

## REMARKS

### **CLAIM REJECTIONS - 35 U.S.C. 103 over De Vuyst et al.:**

Claims 1-19 stand rejected under 35 U.S.C. § 103(a) as obvious over De Vuyst et al. Applicants respectfully traverse this rejection. Applicants assert that the cited reference does not teach, nor does it suggest, the claimed unique invention of the present application. Applicants respectfully request that this ground of rejection be withdrawn. Submitted herewith for the Examiner's consideration is a 132 declaration of the inventor. Applicant respectfully requests that this declaration be entered and made of record.

De Vuyst bacteriocins and Applicant's stress response products is discussed in this § 132 declaration detailing experiments which distinguish Applicant's SRF's and bacteriocins.

Applicant submits that De Vuyst teaches the production of a bacteriocin produced by *Lactobacillus amylovorus* DCE 471 which is bacteriocidal towards closely related *Lactobacillus* strains. (p. 818). De Vuyst further discloses that the bacteriocin-producing lactic acid bacteria could potentially be added to foods to stimulate bacteriocin production. (p. 825).

It is submitted that the Examiner is misinterpreting applicants invention which is not related to bacteriocins. Submitted herewith is a § 132 Declaration of inventor Dr. Marshall which clearly establishes that the SRF compositions of the invention do not include bacteriocins or other compositions with bactericidal properties. The declaration details several experiments conducted using the standard methods in the art and even used by De Vuyst exposing the test strain for bacteriocins, *Lactobacillus helveticus*, ATCC 15009, to the SRF compositions. The results show that the SRF compositions do not exhibit bactericidal activity. The results as depicted in Photograph 1 demonstrate that the preparations of the invention obtained from *L. monocytogenes*, *L. plantarum*, and *E. faecium* DO NOT inhibit growth of *Lactobacillus helveticus*. This is in stark contrast to the bacteriocin Nisin which is shown at the asterisk. Figure 2 shows that stressing *L. monocytogenes*, or even twice stressing *L. plantarum* and *E. faecium* or stressing heat killed *L. plantarum* and *E. faecium* do not result in bacteriocidal activity against *L. helveticus*. Figure 3 demonstrates that bacteriocins against *L. helveticus* are not produced by stressing *L. caseii*, *L. plantarum* or *E. faecium*, again no zones of inhibition are observed from the SRF's. Finally in Figure 4, 7 test strains (5 of *L. plantarum* and 2 of *E. faecium*) were used both as SRF collecting strains and as test strains. Again, the bacteriocin

Nisin inhibited all 7 strains while the SRF's collected from the same strains as well as from *L. casei* did not inhibit growth.

In contrast to the bacteriocin described in De Vuyst, the present invention claims the activation or modulation of the immune system of an animal through the administration of a product produced by bacteria subjected to stress which is then filtered. The SRF's stimulate the immune system and it is the host immune system that battles invading bacteria, not other bacteria or bacteriocins. De Vuyst does not disclose the administration of a bacterial product to an animal which has been filtered from the bacteria, and it further does not teach that the product has been filtered to remove any molecules larger than 10 kDa.

**CLAIM REJECTIONS - 35 U.S.C. 103(a) over De Vuyst et al. in combination with Nanji, Emery or Perdigon:**

Claims 1-15 and 17-19 stand rejected over De Vuyst in combination with Nanji; (which discloses administration of lactic acid bacteria to animals for protection of endotoxin-mediated shock), Emery (which teaches the administration of a bacteriocin to create an immunogenic response); or Perdigon (which discloses lactic acid bacteria as adjuvants).<sup>1</sup> Neither of these references alone or in combination teach, suggest or even mention stress response factors described in Applicant's specification which are distinct, as shown in Applicant's § 132 declaration, from bacteriocins. Applicants invention relates to the unique discovery of SRF's which are neither suggested or taught by De Vuyst.

Nanji teaches a lactobacillus that is acid resistant and able to destroy Gram-negative bacteria. This is a single strain and does not reference applicant's SRF's which are present in all stressed bacteria. In fact Nanji teaches away from the concept that ordinary lactobacilli which do not inhibit *E. coli in vitro* could, when stressed, provide protection against an LPS injection in mice.

The Emery reference teaches bacterial SRP's which are siderophore receptor proteins and are bacterial surface receptors which are similar in acronym only (SRP) to Applicant's factors.

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<sup>1</sup> Claims 1-15 and 17-19 were rejected over De Vuyst in view of Nanji, claim 16 was rejected over De Vuyst in view of Perdigon or Emery.

Perdigon teaches that the health benefits of feeding milk fermented with lactobacilli is due to an interaction between the bacteria and the milk solids. These effects were limited to and based upon the presence of milk, and again teach away from use of stressed bacteria alone.

In light of the above remarks and the amended claims, Applicants assert that neither the suggestion of the claimed unique invention nor the expectation of success is taught in the references cited by the Examiner. In fact, Applicants respectfully submit that any such suggestion would be merely hindsight application of the Applicants specification and claimed invention to the cited references. Applicants respectfully request reconsideration and withdrawal of the rejection to claims 1-19 under 35 U.S.C. 103(a).

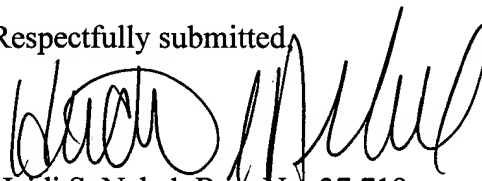
### **CONCLUSION**

In light of the above amendments and remarks, Applicants assert that the claims as amended are in condition for allowance. Applicants respectfully request reconsideration and withdrawal of the above rejections to claims 1-19.

No fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,



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